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EXAMINER

PORTNER, VIRGINIA ALLEN

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**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

<b>Office Action Summary</b>	<b>Application No.</b> 10/577,124	<b>Applicant(s)</b> ROBINSON ET AL.	
	<b>Examiner</b> GINNY PORTNER	<b>Art Unit</b> 1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

#### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

#### Status

- 1) ☒ Responsive to communication(s) filed on 14 September 2009.
- 2a) ☐ This action is **FINAL**.                      2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

#### Disposition of Claims

- 4) ☒ Claim(s) 1,3-5 and 8-40 is/are pending in the application.
- 4a) Of the above claim(s) 9-29,31-36,39-40 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1,3-5,8,30 and 37 is/are rejected.
- 7) ☒ Claim(s) 38 is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

#### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 01 May 2007 is/are: a) ☐ accepted or b) ☒ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

#### Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All    b) ☐ Some \*    c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

#### Attachment(s)

- |  |   |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)            | 4) <input type="checkbox"/> Interview Summary (PTO-413)                 |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)   | Paper No(s)/Mail Date. _____  |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application       |
| Paper No(s)/Mail Date <u>5/2008</u> .  | 6) <input checked="" type="checkbox"/> Other: <u>notice to comply</u> . |

Art Unit: 1645

### **DETAILED ACTION**

Claims 1, 3-5, 8-40 are pending.

#### ***Election/Restrictions/Lack of Unity***

1. The chemical structure, biological function and effect of each of the claimed molecules differ from each other (ie. Proteins are made of amino acids and nucleic acid coding sequences are made up of a series of nucleotide sugar molecules that clearly differ in structure, function and biological effect from amino acids that make up proteins/polypeptides), and the first appearing invention directed to preventing activation of LuxR based upon antibody binding of a signaling molecule is disclosed in the prior art (see US PG-Pub 2003/009585, publication date May 22, 2003, [0169-0170]), therefore the first appearing invention/species does not make a contribution over the prior art, thus the claimed species are not so linked by a special technical feature that makes a contribution over the prior art.

2. With respect to Applicant's assertion that the instant claims no longer read of the reference used to show lack of unity of invention, it is the position of the examiner that claim 1 requires the antibody to prevent the activation of LuxR by its signally molecule, which functionally permits that antibody to bind to the signaling molecule, or to LuxR or may be an antibody that presents a conformation that is a signaling molecule will bind as if it were binding to LuxR (anti-id). Therefore US PG-Pub 2003/009585 still describes the first appearing special technical feature and lack of unity of invention made of record is herein maintained.

Additionally, Applicant's election with traverse of Group I with traverse, and the species of antibody that immunoreacts prevents LuxR or its homologue from being activated, in light of the amendment of the claims, in the reply filed on September 14, 2009 is acknowledged. The traversal is on the ground(s) that that search both Group I and Group II would not be undue burden on the examiner, and asserts that the examination of the both Groups I and II cannot constitute a serious burden.

These arguments have been fully considered but are not found to be persuasive for the reasons below.

First, the classification system has no statutory recognition whether inventions are independent and distinct. For example, each class and subclass is comprised of numerous completely independent and distinct inventions.

Second, MPEP 803 states that restriction is proper between patentably distinct inventions where the inventions are (1) independent or distinct as claimed and (2) a serious search and examination burden is placed on the examiner if restriction is not required.

The term distinct is defined to mean that two or more subjects as disclosed are related, for example, as product and method of use, but are capable of separate manufacture, use or sale as claimed, and are patentable over each other (see MPEP 802.1). In the instant situation, the inventions of Groups I-IX, and I and II are drawn to distinct inventions which are related as separate products capable of separate functions. Restrictions between the inventions is deemed to be proper for the reason previously set forth.

In regard to burden of search and examination, MPEP 803 states that a burden can be shown if the examiner shows either separate classification, different field of search or separate status in the art. Antibodies may be humanized, anti-id, chimeric, monoclonal, or polyclonal, all of which do not have the same structure and biological functions, nor need not evidence the same binding specificities or affinities, and may or may not be used in a method of regulating quorum sensing in a bacteria. In the instant case a burden has been established in showing that the inventions of Groups I-IX are classified separately necessitating different searches of issued US Patents. However, classification of subject matter is merely one indication of the burdensome nature of search. The literature search, particularly relevant in this art, is not co-extensive, because for example antibody production need not be co-extensive with a method of regulation of a LuxR homolog. Additionally, it is submitted that the inventions of Groups have acquired a separate status in the art. Clearly different searches and issues are involved in the examination of each Group.

For these reasons the restriction requirement is deemed to be proper and is therefore made Final.

### **Ochiai/Brouwer Rejoinder**

The examiner has required restriction between product and process claims. Where applicant elects claims directed to the product, and a product claim is subsequently found allowable, withdrawn process claims that depend from or otherwise include all the limitations of the allowable product claim will be rejoined in accordance with the provisions of MPEP § 821.04. **Process claims that depend from or otherwise include all the limitations of the patentable product** will be entered as a matter of right if the amendment is presented prior to final rejection or allowance, whichever is earlier. Amendments submitted after final rejection

Art Unit: 1645

are governed by 37 CFR 1.116; amendments submitted after allowance are governed by 37 CFR 1.312.

In the event of rejoinder, the requirement for restriction between the product claims and the rejoined process claims will be withdrawn, and the rejoined process claims will be fully examined for patentability in accordance with 37 CFR 1.104. Thus, to be allowable, the rejoined claims must meet all criteria for patentability including the requirements of 35 U.S.C. 101, 102, 103, and 112. Until an elected product claim is found allowable, an otherwise proper restriction requirement between product claims and process claims may be maintained. Withdrawn process claims that are not commensurate in scope with an allowed product claim will not be rejoined. See A Guidance on Treatment of Product and Process Claims in light of *In re Ochiai*, *In re Brouwer* and 35 U.S.C. § 103(b), 1184 O.G. 86 (March 26, 1996). Additionally, in order to retain the right to rejoinder in accordance with the above policy, Applicant is advised that the process claims should be amended during prosecution either to maintain dependency on the product claims or to otherwise include the limitations of the product claims. **Failure to do so may result in a loss of the right to rejoinder.**

Further, note that the prohibition against double patenting rejections of 35 U.S.C. 121 does not apply where the restriction requirement is withdrawn by the examiner before the patent issues. See MPEP § 804.01.

1. Claims 1, 3-5, 8, 30, 37-38 are under consideration; all other claims stand withdrawn from consideration as being drawn to a non-elected invention.

#### ***Priority***

1. Receipt is acknowledged of papers submitted under 35 U.S.C. 119(a)-(d), which papers have been placed of record in the file.

#### ***Information Disclosure Statement***

2. The information disclosure statement filed May 27, 2008 has been considered.

***Claim Objections***

2. Claim 38 depends from both claims 12 and 37 simultaneously and is a "Use" claim which is a non-statutory category of invention. Claim 38 is objected to under 37 CFR 1.75(c) as being in improper form because a multiple dependent claim must depend from prior claims in the alternative and not simultaneously. See MPEP § 608.01(n). Accordingly, the claim 38 not been further treated on the merits.

***Drawings***

3. The drawings are objected to as failing to comply with 37 CFR 1.84(p)(5) because they include the following reference character(s) not mentioned in the description: The SEQ ID NOs are not provided in the Brief Description of the Drawing for the sequences shown in Figure 1. Corrected drawing sheets in compliance with 37 CFR 1.121(d), or amendment to the specification to add the reference character(s) in the description in compliance with 37 CFR 1.121(b) are required in reply to the Office action to avoid abandonment of the application. Any amended replacement drawing sheet should include all of the figures appearing on the immediate prior version of the sheet, even if only one figure is being amended. Each drawing sheet submitted after the filing date of an application must be labeled in the top margin as either "Replacement Sheet" or "New Sheet" pursuant to 37 CFR 1.121(d). If the changes are not accepted by the examiner, the applicant will be notified and informed of any required corrective action in the next Office action. The objection to the drawings will not be held in abeyance.

***Claim Rejections - 35 USC § 101***

4. 35 U.S.C. 101 reads as follows:

Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

5. Claim 30 provides for the use of methods of claim 1 or 3, but, since the claim does not set forth any steps involved in the method/process, it is unclear what method/process applicant is intending to encompass. A claim is indefinite where it merely recites a use without any active, positive steps delimiting how this use is actually practiced.

Claim 30 is rejected under 35 U.S.C. 101 because the claimed recitation of a use, without setting forth any steps involved in the process, results in an improper definition of a process, i.e., results in a claim which is not a proper process claim under 35 U.S.C. 101. See for example *Ex parte Dunki*, 153 USPQ 678 (Bd.App. 1967) and *Clinical Products, Ltd. v. Brenner*, 255 F. Supp. 131, 149 USPQ 475 (D.D.C. 1966).

***Claim Rejections - 35 USC § 102***

3. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

(c) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

Art Unit: 1645

The changes made to 35 U.S.C. 102(e) by the American Inventors Protection Act of 1999 (AIPA) and the Intellectual Property and High Technology Technical Amendments Act of 2002 do not apply when the reference is a U.S. patent resulting directly or indirectly from an international application filed before November 29, 2000. Therefore, the prior art date of the reference is determined under 35 U.S.C. 102(e) prior to the amendment by the AIPA (pre-AIPA 35 U.S.C. 102(e)).

4. Claim 1, 3-5, 8, 30, 37 rejected under 35 U.S.C. 102(b) as being anticipated by Kende et al US PG-Pub 2003/0095985.

5. Kende et al disclose the instantly claimed invention directed to a method that modulates or inhibits the activation of a LuxR homolog, specifically LasR, wherein the modulation is achieved by administering an antibody and sequestering the quorum sensing signaling molecules by forming antibody/signaling molecule complexes associated with a gram negative bacterium,

6. the antibody being either a monoclonal or polyclonal antibody, and the signaling molecule being specific to the LasR ([0016] In a specific embodiment, the carrier molecule of the immunogenic conjugate has at least one amine group, the autoinducer has an N-acyl homoserine lactone structure, and the conjugate is the reductive amination product of the carrier molecule and the autoinducer), a homoserine lactone (see Kende et al, claims 22-34 and [0167-170]). Kende et al anticipates the instantly claimed invention as now claimed.

“Claim 22. A method of treating or preventing an infectious disease in a subject comprising **administering an amount of an antibody** or fragment thereof which specifically binds an autoinducer of a Gram negative bacteria of a compound of Formula (I): 15where X is O, S, N--(C.sub.1-C.sub.6) alkyl, NR.sup.2, N-phenyl; Y is C.sub.1-C.sub.6 straight or branched alkyl, C.sub.1-C.sub.6 straight or branched alkenyl, C.sub.1-C.sub.6 straight or branched alkynyl; Z is C.dbd.O, C.dbd.S, CHOH, C.dbd.N--NR.sup.1, C.dbd.N--OH, C.sub.1-C.sub.8 straight or branched alkyl, C.sub.1-C.sub.8 straight or branched alkenyl, C.sub.1-C.sub.8 straight or branched alkynyl; L is C.sub.1-C.sub.18 straight or branched alkyl, C.sub.1-C.sub.18 straight or branched alkenyl, C.sub.1-C.sub.18 straight branched alkynyl, or --CO.sub.2H, --CO.sub.2R.sup.1, --CHO, --C.ident.N, --N.dbd.C.dbd.O, --N.dbd.C.dbd.S, OH, OR.sup.1, --CH.dbd.CH--CH.sub.2Br, --CH.dbd.CH--CH.sub.2Cl, --SAC or SH, where R.sup.1 is C.sub.1-C.sub.6 straight or branched alkyl, m is 0 or 1; z is 0 or 1; R.sup.2 is H, C.sub.1-C.sub.6 straight or branched alkyl, C.sub.1-C.sub.6 straight or branched alkenyl or C.sub.1-C.sub.6 straight or branched alkynyl, or CO.sub.2H; and Q is CH or N; and n is 0-3 with the proviso that when n is 0, X is N-(C.sub.1-C.sub.6 alkyl) or N-phenyl, in which said amount is effective to treat or prevent said infectious disease.

23. The method according to claim 22 wherein said subject is a human.



Art Unit: 1645

24. The method according to claim 22 wherein said antibody is administered orally, intradermally, intramuscularly, intraperitoneally, intravenously, subcutaneously, or intranasally.

25. The method of claim 22 in which the infectious disease is caused by a Gram negative bacteria.

27. A pharmaceutical composition comprising an antibody or fragment thereof which specifically binds an autoinducer produced by a Gram negative bacteria; and a pharmaceutically acceptable carrier.

28. The pharmaceutical composition of claim 27 in which the autoinducer is a compound of Formula (I):  $17$  where X is O, S, N--(C.sub.1-C.sub.6) alkyl, NR.sup.2, N-phenyl; Y is C.sub.1-C.sub.6 straight or branched alkyl, C.sub.1-C.sub.6 straight or branched alkenyl, C.sub.1-C.sub.6 straight or branched alkynyl; Z is C.dbd.O, C.dbd.S, CHOH, C.dbd.N--NR.sup.1, C.dbd.N--OH, C.sub.1-C.sub.8 straight or branched alkyl, C.sub.1-C.sub.8 straight or branched alkenyl, C.sub.1-C.sub.8 straight or branched alkynyl; L is C.sub.1-C.sub.18 straight or branched alkyl, C.sub.1-C.sub.18 straight or branched alkenyl, C.sub.1-C.sub.18 straight branched alkynyl, or --CO.sub.2H, --CO.sub.2R.sup.1, --CHO, --C.ident.N, --N.dbd.C.dbd.O, --N.dbd.C.dbd.S, OH, OR.sup.1, --CH.dbd.CH--CH.sub.2Br, --CH.dbd.CH--CH.sub.2Cl, --SAc or SH, where R.sup.1 is C.sub.1-C.sub.6 straight or branched alkyl, m is 0 or 1; z is 0 or 1; R.sup.2 is H, C.sub.1-C.sub.6 straight or branched alkyl, C.sub.1-C.sub.6 straight or branched alkenyl or C.sub.1-C.sub.6 straight or branched alkynyl, or CO.sub.2H; and Q is CH or N; and n is 0-3 with the proviso that when n is 0, X is N-(C.sub.1-C.sub.6 alkyl) or N-phenyl; and a pharmaceutically acceptable carrier.

29. The pharmaceutical composition of claim 27 which the antibody is **a monoclonal antibody**.

30. The pharmaceutical composition of claim 27 in which the autoinducer comprises N-(3-oxododecanoyl)-L-homoserine lactone, N-(butanoyl)-L-homoserine lactone, N-hexanoyl-homoserine lactone, N-(3-oxohexanoyl)-homoserine lactone, N-.beta.(hydroxybutyryl)-homoserine lactone, N-(3-oxooctanoyl)-L-homoserine lactone, or N-(3R-hydroxy-cis-tetradecanoyl)-L-homoserine lactone.

31. The pharmaceutical composition of claim 27 in which the autoinducer is N-(3-oxododecanoyl)-L-homoserine lactone or N-(butanoyl)-L-homoserine lactone.

32. The pharmaceutical composition of claim 27 in which the autoinducer is covalently conjugated or otherwise bound to a carrier molecule.

33. The pharmaceutical composition of claim 32 in which the carrier molecule is selected from the group consisting of bovine serum albumin, chicken egg ovalbumin, keyhole limpet hemocyanin, tetanus toxoid, diphtheria toxoid, and thyroglobulin.

34. The pharmaceutical composition of claim 27 in which the autoinducer is produced by a **Gram negative bacteria** comprising *Aeromonas hydrophila*, *Agrobacterium tumefaciens*, *Burkholderia cepacia*, *Chromobacterium violaceum*, *Enterobacter agglomerans*, *Erwinia stewartii*, *Erwinia carotovora*, *Escherichia coli*, *Nitrosomas europea*, *Photobacterium fischeri*, *Pseudomonas aeruginosa*, *Pseudomonas aureofaciens*, *Rhizobium leguminosarum*, *Serratia liquefaciens*, or *Vibrio harveyi*.

#### 0167] 7.3 Neutralization of PAI with Antibodies

[0168] In Vitro neutralization of PAI-1 with anti-PAI-1 polyclonal antibodies. Immune serum, collected in Section 7.2, were tested for neutralization of PAI-1 in an in vitro bioassay. The E. coli MG4 strain, containing the lysogen .lambda.I.sub.14 (a lasI/lasZ transcriptional fusion) and pPCS1 (a plasmid expressing lasR), was used as a positive control to detect the presence of PAI-1. Normally, when PAI-1 is added to cultures it can bind LasR, the PAI-1 specific transcriptional activator protein, and form a complex that is able to induce transcription of the lasI/lasZ fusion protein. The production of .beta.-galactosidase in this system is a quantitative and direct measure of the activation induced by PAI-1. The expression construct, .lambda.I.sub.14-MG4 (PPCS1), has been shown to have

Art Unit: 1645

half-maximal expression at PAI-1 concentrations of 100 pM and can be activated at PAI-1 concentrations as low as 10 pM (Seed et al., 1995, J. Bacteriol. 177:654-59, which is hereby incorporated by reference).

[0169] A test sample containing 100 pM of PAI-1 was preincubated for one hour at 37.degree. C. with a 1:10 dilution of serum from mice immunized with a PAI-1 conjugate or a Compound D conjugate (both contain anti-PAI-1 polyclonal antibodies). Control samples containing 100 pM PAI-1 were incubated at 37.degree. C. for one hour with a 1:10 dilution of preimmune serum or an equal volume of PBS. Following preincubation, the samples were tested in an E. coli bioassay using .lambda..sub.14-MG4 (pPCS1). When the bacteria in each sample reached an OD600 of 0.8-1.0 the samples were assayed for the production of .beta.-galactosidase which was expressed as Miller Units of activity. The test samples preincubated with serum from immune mice displayed a 70% reduction in .beta.-galactosidase production as compared to control sample preincubated with nonimmune serum (FIG. 2). These results indicate that PAI-1 conjugates or related conjugates (Compound D) can induce the production of polyclonal antibodies that can react with PAI-1 and inhibit its interaction with LasR.

[0170] Mice immunized with the PAI-1 conjugate were used to produce monoclonal antibodies. These antibodies were screened using an ELISA utilizing a PAM-1/OVA conjugate. Positive clones were tested in a Pseudomonas aeruginosa bioassay. PAO-JP2 (bearing the lasI/rhII double deletion) produces no PAI-1 but retains the ability to produce LasR. When PAI-1 is added exogenously, it can bind to LasR and induce the transcription of lasI. Test samples containing 40 nM PAI (the concentration that stimulates half-maximal activity in this assay) were preincubated at 37.degree. C. with anti-PAI-1 monoclonal antibody (618.4). Control samples containing 40 nM PAI-1 were preincubated at 37.degree. C. with an equal volume of PBS. Following preincubation, the samples were tested in a Pseudomonas aeruginosa bioassay using PAO-JP2 containing a plasmid with a lasI/LacZ fusion. When the bacteria reached an OD<sub>600</sub> of 0.8-1.0, the samples were assayed for the production of .beta.-galactosidase, which was expressed as Miller Units of activity. The test sample preincubated with anti-PAI-1 monoclonal antibody 618.4 displayed an 80% reduction in the production of .beta.-galactosidase as compared to the control sample (FIG. 3). These results indicate that in Pseudomonas aeruginosa antibodies specific for PAI-1 can inhibit PAI-1 activation of LasR and transcription of other genes that are regulated by LasR/PAI-1.

7. Claims 1,3,5 8, 30,37 are rejected under 35 U.S.C. 102(e) as being anticipated by Ulrich et al (US PG Pub 2004/0171020, filing date July 15, 2002).

Ulrich et al disclose the instantly claimed invention directed to a method of modulating or inhibiting LuxR activation with an antibody, the methods

contacting a LuxR homolog or LuxR signaling molecule with antibodies (see claims 40, 41 and 42, 48) directed thereto to reduce (modulate) or inhibit the LuxR activation (referred to as the synthase transcriptional regulator), wherein the antibodies are either polyclonal or monoclonal antibodies, and are specific for the gram negative bacterium [0002] Burkholderia mallei ("the etiologic agent of glanders disease is a gram-negative, oxidase positive, nonmotile

Art Unit: 1645

bacillus that is an obligate animal pathogen"; [0010] *B. mallei* contains two AHS genes (*bmaI1* and *bmaI2*) and four LuxR homologues (*bmaR1*, *bmaR3*, *bmaR4*, *bmaR5*)

[0021] It is a further object of the present invention to provide an antibody to the above-described recombinant proteins.

[0022] It is yet another object of the present invention to provide a method for detecting AHS in a sample comprising:

[0023] (i) contacting a sample with antibodies which recognize AHS; and

[0024] (ii) detecting the presence or absence of a complex formed between AHS and antibodies specific therefor.

[0025] It is yet another object of the present invention to provide a method for detecting AHS transcriptional regulator in a sample comprising:

[0026] (i) contacting a sample with antibodies which recognize AHS transcriptional regulator; and

[0027] (ii) detecting the presence or absence of a complex formed between AHS transcriptional regulator and antibodies specific therefore.

[0070] The recombinant or fusion protein can be used as a diagnostic tool and in a method for producing antibodies against AHS or AHS transcriptional regulator, detectably labeled and unlabeled, or as a bait protein in an assay to isolate proteins or target gene which interact with AHS or AHS transcriptional regulator. The transformed host cells can be used to analyze the effectiveness of drugs and agents which inhibit AHS or AHS transcriptional regulator function, such as host proteins or chemically derived agents or natural or synthetic drugs and other proteins which may interact with the cell to down-regulate or alter the expression of AHS or AHS transcriptional regulator, or its cofactors.

[0071] In another embodiment, the present invention relates to monoclonal or polyclonal antibodies specific for the above-described recombinant proteins (or polypeptides). For instance, an antibody can be raised against a peptide described above, or against a portion thereof of at least 10 amino acids, preferably, 11-15 amino acids. Persons with ordinary skill in the art using standard methodology can raise monoclonal and polyclonal antibodies to the protein (or polypeptide) of the present invention, or a unique portion thereof. Material and methods for producing antibodies are well known in the art (see for example Goding, in, Monoclonal Antibodies: Principles and Practice, Chapter 4, 1986).

[0093]... antibodies,... capable of reducing or inhibiting the synthase or the synthase transcriptional regulator, that is reducing or inhibiting either the expression, production or activity of these proteins, such as antagonists, can be provided as an isolated and substantially

Art Unit: 1645

purified protein, or as part of an expression vector capable of being expressed in the target cell such that the synthase-reducing or inhibiting agent is produced. In addition, co-factors such as various ions, i.e.  $\text{Ca}^{2+}$  or factors which affect the stability of the enzyme can be administered to modulate the expression and function of synthase. These formulations can be administered by standard routes. In general, the combinations may be administered by the topical, transdermal, intraperitoneal, oral, rectal, or parenteral (e.g. intravenous, subcutaneous, or intramuscular) route. In addition, synthase-inhibiting compounds may be incorporated into biodegradable polymers being implanted in the vicinity of where drug delivery is desired, for example, at the site of infection or implanted so that the synthase-inhibiting compound is slowly released systemically. The biodegradable polymers and their use are described, for example, in detail in Brem et al.(1991) J. Neurosurg. 74, 441-446. These compounds are intended to be provided to recipient subjects in an amount sufficient to effect the inhibition of synthase. Similarly, agents which are capable of negatively affecting the expression, production, stability or function of synthase, are intended to be provided to recipient subjects in an amount sufficient to effect the inhibition of synthase. An amount is said to be sufficient to "effect" the inhibition or induction of synthase if the dosage, route of administration, etc. of the agent are sufficient to influence such a response.

[0094] In providing a subject, specifically equine or human, with agents which modulate the expression or function of synthase to a recipient patient, the dosage of administered agent will vary depending upon such factors as the patient's age, weight, height, sex, general medical condition, previous medical history, etc. In general, it is desirable to provide the recipient with a dosage of agent which is in the range of from about 1 pg/kg to 10 mg/kg (body weight of patient), although a lower or higher dosage may be administered.

[0095] A composition is said to be "pharmacologically acceptable" if its administration can be tolerated by a recipient patient. Such an agent is said to be administered in a "therapeutically effective amount" if the amount administered is physiologically significant. An agent is physiologically significant if its presence results in a detectable change in the physiology of a recipient patient.

[0096] The compounds of the present invention can be formulated according to known methods to prepare pharmaceutically useful compositions, whereby these materials, or their functional derivatives, are combined in admixture with a pharmaceutically acceptable carrier vehicle. Suitable vehicles and their formulation, inclusive of other human proteins, e.g., human serum albumin, are described, for example, in Remington's Pharmaceutical Sciences [16th ed., Osol, A. ed., Mack Easton Pa. (1980)]. In order to form a pharmaceutically acceptable composition suitable for effective administration, such compositions will contain an effective amount of the above-described compounds together with a suitable amount of carrier vehicle.

[0097] Additional pharmaceutical methods may be employed to control the duration of action. Control release preparations may be achieved through the use of polymers to complex or absorb the compounds. The controlled delivery may be exercised by selecting appropriate macromolecules (for example polyesters, polyamino acids, polyvinyl, pyrrolidone, ethylenevinylacetate, methylcellulose, carboxymethylcellulose, or protamine sulfate) and the

Art Unit: 1645

concentration of macromolecules as well as the method of incorporation in order to control release. Another possible method to control the duration of action by controlled release preparations is to incorporate the compounds of the present invention into particles of a polymeric material such as polyesters, polyamino acids, hydrogels, poly(lactic acid) or ethylene vinylacetate copolymers. Alternatively, instead of incorporating these agents into polymeric particles, it is possible to entrap these materials in microcapsules prepared, for example, interfacial polymerization, for example, hydroxymethylcellulose or gelatin-microcapsules and poly(methylmethacrylate)-microcapsules, respectively, or in colloidal drug delivery systems, for example, liposomes, albumin microspheres, microemulsions, nanoparticles, and nanocapsules or in macroemulsions. Such techniques are disclosed in Remington's Pharmaceutical Sciences (1980).

Ulrich et al inherently anticipates the instantly claimed invention as now claimed, because while the reference does not recite the term "biofilm inhibition", the reference carries out the claimed method steps with antibodies specific for a LuxR homolog or antibodies specific for LuxR signaling molecules for the purpose of modulating gram negative bacterial growth, or inhibition of bacterial growth. The inhibition of bacterial growth is the same or equivalent process as inhibiting biofilm formation as bacterial growth is the source of biofilm formation and the antibodies of Ulrich et al serve to inhibit bacterial growth.

### ***Sequence Requirements***

This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 C.F.R. § 1.821(a)(1) and (a)(2). However, this application fails to comply with the requirements of 37 C.F.R. §§ 1.821-1.825 for the reason(s) set forth on the attached Notice To Comply With Requirements For Patent Applications Containing Nucleotide Sequence And/Or Amino Acid Sequence Disclosures.

Full compliance with the sequence rules is required in response to this office action. A complete response to this office action should include both compliance with the sequence rules

Art Unit: 1645

and a response to the instant office action set forth below. Failure to fully comply with **both** these requirements in the time period set forth in this office action will be held non-responsive.

This application contains sequence disclosures at pages 5, paragraph 3 and page 24, last line that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 C.F.R. § 1.821(a)(1) and (a)(2). However, the fails to comply with the requirements of 37 CFR 1.821 through 1.825 for the reason(s) set forth below: Nucleic acid sequences of 10 or more nucleotides and amino acid sequences of 4 or more residues need to be designated with a sequence identifier. Wherein attention is directed to paragraph(s) §1.82 (c) and (e). Although an examination of this application on the merits can proceed without prior compliance, compliance with the Sequence Rules is required for the response to this Office action to be complete.

Claim 11 is objected to for not complying with the requirements of 37 CFR 1.821. The claims contain sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR 1.821(a)(1) and (a)(2). However, the fails to comply with the requirements of 37 CFR 1.821 through 1.825 for the reason(s) set forth below: Nucleic acid sequences of 10 or more nucleotides and amino acid sequences of 4 or more residues need to be designated with a sequence identifier. Although an examination of this application on the merits can proceed without prior compliance, compliance with the Sequence Rules is required for the response to this Office action to be complete. Applicants must correct the sequence submissions in the mentioned claims.

Examiner would like to point out that there is no information with regards to SEQ ID NO for sequence set forth in figure 1 and claim 11:

- ❖ the amino acid sequences present in Figure 1 should have SEQ ID No described , in the Brief Description of the Drawings (Brief Description on page 18, Figure 1 is incomplete as the SEQ ID NOs are not present in Figure 1 or in the Brief Description of the drawings as required by the sequence rules). If the Drawings contain amino acid sequences that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 C.F.R. § 1.821(a)((1) and (a)(2) then the Brief Description of the Drawings needs to state the SEQ ID NO: for the nucleotide and/or amino acid sequences. Unless the appropriate SEQ ID NO: accompanies the nucleotide and/or amino acid sequences in the actual Drawing sheet.
- ❖ Claim 11 recites an amino acid sequence that requires a SEQ ID NO.

***Conclusion***

***This is a non-final action.***

8. The prior art made of record and not relied upon is considered pertinent to applicant's disclosure. Various references are being cited to show LuxR proteins and antibodies.

9. Any inquiry concerning this communication or earlier communications from the examiner should be directed to GINNY PORTNER whose telephone number is (571)272-0862. The examiner can normally be reached on flextime, but usually M-F, alternate Fridays off.

Art Unit: 1645

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Robert Mondesi can be reached on 571-272-0956. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Ginny Portner/  
Examiner, Art Unit 1645  
December 23, 2009

/Robert B Mondesi/  
Supervisory Patent Examiner, Art Unit 1645

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